A study on glucose tolerance test in young sputum positive tuberculosis patients

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Abstract

Introduction: Diabetes mellitus and Tuberculosis are among the most prevalent chronic diseases in India. The correlation and coexistence of both the diseases are very important as they influence the clinical course and therapeutics of each other.

Material and Methods: It was a cross sectional study conducted on 122 patients of newly diagnosed young sputum positive tuberculosis patients visiting a tertiary care hospital. Selected socio-demographic, laboratory and radiological data were elicited from these patients and recorded in the proforma. After GTT, patients were grouped according to ADA 2003 recommendations of hyperglycaemia into Normal, IFG, IGT and DM was done.

Observation and results: The total number of patients with abnormal blood sugar values (IFG, + IGT + DM) account for 53.28% of the study group. IGT is significantly high in TB population (31%) when compared to (14%) that in normal population and p value is significant <0.05.On radiological examination, a total of 61% of the study group shows upper zone involvement and the lesions were mostly infiltrates. There was no statistical correlation between IGT or DM and increased BMI.IGT and DM was more among urban population and this was statistically significant.

Conclusions: In view of the increased prevalence of diabetes mellitus in tuberculosis population it is suggested that all tuberculosis patients should be evaluated clinically and biochemically for diabetes mellitus as detection and control of diabetes mellitus will help to achieve better tuberculosis control.

Keywords: ADA: American Diabetic Association, IFG: Impaired Fasting Glycaemia, IGT: Impaired Glucose tolerance, OGTT: Oral Glucose Tolerance test, DM; Diabetes Mellitus

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Introduction

Tuberculosis and Diabetes mellitus are among the top rated diseases in the Indian population, with significant effects on morbidity and mortality of the community, and producing a great impact on the economy of the society. To find out the correlation and coexistence of both the diseases are very important as they influence the clinical course and therapeutics of each other. It has been postulated that in the context of economic development, a country's health issues will evolve from infectious to noninfectious diseases. In reality, this transition more commonly simply adds chronic conditions to a public health system already burdened by infectious disease. In many settings, this process will result in the convergence of two epidemics: Diabetes and Tuberculosis[1].

There is now recognition of an explosive epidemic called Diabetes in India and in this pandemic invasion of Diabetes, the diagnosed cases form just a tip of the iceberg. WHO has projected that maximum increase in diabetes would occur in India[2].Tuberculosis and diabetes frequently coexist together and there is a growing amount of evidence of one disease fueling the other.

Symptoms of one disease often mimic those of the other. Loss of weight, loss of appetite and lassitude are common to both diseases. The association is more common among those above 40 yrs of age.

Diabetes appears to have an induction and aggravating effect on tuberculosis. Tuberculosis was found to be more pronounced in diabetes, had more pronounced radiological signs, treatment failures and deaths were also frequent. Diabetes mellitus has been reported to modify the presenting features of pulmonary tuberculosis but their conjoint presence does not alter the symptomatology, bacteriology and tuberculin reaction. Some studies have even indicated that MDR-TB is more common in diabetes than in non diabetic population.

Since simple tests like sputum analysis and blood sugar estimation will make a definitive diagnosis of pulmonary tuberculosis and diabetes mellitus respectively, the knowledge of the degree of coexistence of these diseases should make the treating doctor to search for the other disease when one is diagnosed.

The diagnosis of coexisting diabetes in TB patients will also help in early treatment of the same and retardation of various complications of diabetes like renal impairment, CAD, stroke etc. which are important

factors adversely affecting prognosis of patients with tuberculosis sequelae if they do occur.

Currently in India approximately 20 million people suffer from diabetes but less than 12% receive pharmacological treatment. It has been projected that by the year 2025, there would be 57.2 million diabetics in India[2]. Diabetics are high risk group for tuberculosis, especially insulin dependent patients whose risk is about 38 times higher than the general population.

Many studies have explored the association between diabetes and tuberculosis. In developed countries, studies dating to the first half of the past century demonstrated considerable increase in the frequency of tuberculosis among patients with diabetes although the proportion with comorbidity has ranged widely from 1.0[3] to 9.3%[4]. Other studies have shown a higher frequency of diabetes among individuals with tuberculosis[5,6]. Similar results were found in the few studies that have addressed this association in developing countries.

Hence an attempt has been made through this study to identify the prevalence of IGT and Diabetes Mellitus among young sputum positive pulmonary tuberculosis patients in Madurai and to find out the significance of the same.

Aims and objectives

1. To assess the prevalence of diabetes and IGT among newly detected young sputum positive tuberculosis patients.
2. To assess the radiological profile of such cases.
3. To analyze the gender difference.
4. To suggest workable guidelines to detect diabetes mellitus among tuberculosis population.

Materials and Methods

It was a cross sectional study conducted in a tertiary care hospital by the department of Medicine in collaboration with Department of Thoracic Medicine and Department of Diabetology. Approval from the Institutional ethics committee was taken. A total of one hundred and twenty two consecutive patients of newly diagnosed young sputum positive tuberculosis patients attending the outpatient clinic of Department of Thoracic Medicine, Government Rajaji Hospital, Madurai were included for this present study on the basis of a set of inclusion and exclusion criteria out of 780 patients.

Inclusion criteria: Newly diagnosed young (age 25-45 years) sputum positive tuberculous patients of both sexes who were conscious cooperative and free of overt comorbid illness were considered for the study.

Exclusion criteria: Patients who had any of the following were excluded from the study.

1. Age <25 - > 45 Years
2. HIV positive
3. Known diabetic
4. BMI >25
5. Hypertensives
6. Patient with thyroid or adrenal disorders
7. Acute conditions: Acute myocardial infarction, Acute CVA, Acute medical emergencies
8. Patients with malignancy
9. Bed ridden patients
10. Psychiatric patients
11. Uncooperative patients
12. Pregnant women
13. Women on oral contraceptive pills
14. Alcoholic / smokers
15. Patients who are on -steroids, β blockers, diuretics etc.
16. Family history of diabetes

The study was conducted for a year from 1st August 2005-July 2006

Selected sociodemographic, laboratory and radiological data were elicited from these patients and recorded in the proforma.

1. **Socio demographic data**
   - Age
   - Sex
   - Domicile – Rural / Urban
2. **BMI**
3. **Radiological data**
   Chest X ray of all patients were taken and reports included.
4. **Laboratory Data**
   - GTT – was done in all patients. Blood sugar was measured using COBAS autoanalyser.
   - Sputum for acid fast bacilli by Ziehl Nielsen technique

There was no conflict of interest in the study and Statistical analysis was done using Chi square test and t test with SPSS 16 version.

Definitions Used for the Study Purpose

1. **Sputum positive tuberculosis (RNTCP guidelines):** Patients with at least 2 sputum samples positive for AFB by microscopy and those with one sputum sample positive and radiological abnormalities consistent with active pulmonary tuberculosis.

2. Age definition by WHO

Young	25-45 Years
Middle age	45-65 Years
Elderly	>65Years

3. **OGTT[7]:** The OGTT should be administered in the morning after the patients had at least 3 days of unrestricted diet (>150 g of carbohydrate daily) and usual physical activity. The test should be preceded by an overnight fast of 10 to 16 hours, during which the patient may drink water. The patient may

not smoke during the test. Factors that may influence interpretation of the results of the test should be recorded (e.g., medications, inactivity, infection). Such factors should be taken into account in interpreting the results of the test.

After the fasting blood sample is collected, the subject should drink 75g of anhydrous glucose (or partial hydrolysates of starch with an equivalent carbohydrate content) in 150 to 300 of water over the course of 5 minutes. Blood samples are drawn before (fasting) and 2 hours after the load.

4. ADA 2003 recommendations of hyperglycemia[7]

Table 1

Fasting Plasma Glucose Level				
	Normal	**Impaired**	**Diabetes**	
2-Hour postload plasma glucose level	<100mg/dl <5.5 mmo1/L	100-125 mg/dl 5.6-6.9 mmol/L	≥126 mg/dl ≥ 7.0 mmol/L	Not done
<140 mg/dl (<7.8 mmol/L)	Normal	IFG	Diabetes	Normal
140-199 mg/dl (7.8-11.0 mmol/L)	IGT	IFG/IGT	Diabetes	IGT
≥ 200 mg/dl (≥11.1 mmol/L	Diabetes	Diabetes	Diabetes	Diabetes
Not done	Normal	IFG	Diabetes	Unknown

5. BMI = $\frac{\text{Weight in Kg}}{\text{Height in m}^2}$

6. X-ray Zones –

- Upper Zone - 1st and 2nd intercostal space
- Mid Zone - 3rd and 4th intercostal spaces
- Lower Zone - Rest of intercostal sp

Results

Blood Sugar Analysis

Table 2: GTT Results

ADA grading	**Male**	**Female**	**Total**
N(Normal)	36 (29.5%)	21(17.21%)	57(46,72%)
IFG	3(2.4%)	3(2.4%)	6(4.9%)
IGT	27(22.13%)	11(9.0%)	38(31.14%)
DM	15(12.29%)	6(4.9%)	21(17.21%)

This study revealed that 53.28% of the patients had abnormal blood sugar values in the form of IFG(Impaired Fasting Glycaemia)– 4.9% , IGT(Impaired Glucose tolerance) – 31.14%, DM(Diabetes Mellitus)- 17% where as prevalence of IGT in normal population in Tamilnadu – was 14% and DM was 13.4% .

Table 3: Statistical analysis of IGT results

ADA Grade	**Proportion**		**t value**	**p value**
	Study Group	**Normal Population**		
IGT	0.3115	0.1400	3.1507	0.0011
DM	0.1721	0.1350	0.7683	0.4431

The IGT in the study group was higher than the normal population with definite statistical significance $p < 0.05$. But Diabetes in the study group didn't show any statistical significance when compared to normal population ($p > 0.05$).This table shows that the prevalence of IGT is more than diabetes in the study group which is statistically significant($p = 0.0106$).

Table 4: Age and Gender wise Break up of OGTT results

Age	Males				Females			
	N	IFG	IGT	DM	N	IFG	IGT	DM
25-30	12	1	5	1	11	1	2	1
31-35	5	1	5	1	3	0	5	0
36-40	9	0	5	2	4	0	3	0
41-45	10	1	12	11	3	1	1	5

Analysis of age in different groups with reference to the GTT results revealed that 55.2% of IGT (n=38) and 85.7% of DM (n=21) occurred in the 36-45 age group showing that increased coexistence of TB and IGT and DM in this age group. There is no statistically significant difference in the IGT, or DM among males / females and P value > 0.05 in significant.

Analysis of Radiological Finding

Table 5: Correlation of X-ray zone involvement with GTT results

Zone	N	IFG	IGT	DM
Upper Zone	34	3	28	10
Mid. Zone	3	0	0	2
Lower Zone	4	2	3	1
Multiple Zone	9	1	5	7

61% of the study group showed upper zone involvement and when correlated with GTT results. 59% of N (n=59) 50% of IFG (n=6), 73.6% IGT (n=38) and 47.6% of DM (n=21) cases showed upper zone involvement. This clearly shows that upper zone lesion predominate in both IGT and DM in both genders and the p value is statistically significant (< 0.05).

Table 6: Statistical Analysis of X-ray zone involvement (Upper zone) – correlated with IGT and DM

	Male	Female	Total
DM	0.1406	0.1250	0.1354
IGT	0.3750	0.3438	0.3646
P	0.0021*	0.0365*	0.0002*

Table 7: Analysis of Lesions in chest X-ray

Lesions	Right	Left	Total	Percentage
Infiltrate	61	41	102	72.34%
Consolidation	6	3	9	6.38%
Cavity	18	3	21	14.89%
Effusion	5	2	7	4.96%
Hydropneumothorax	2	2	4	2.13%
Total	92	51	142*	

*Total no of lesions is more than sample size because multiple lesions were observed in some patients. Infiltrates were the commonest lesion documented (72.34%) in the study group.

Table 8: Analysis of lesions in X-ray according to Age – Right

Age group	Infiltrates	Cavity	Consolidation	Effusion	Hydropneumothorax
25-30	18	4	1	0	1
31-35	12	1	1	2	0
36-40	7	5	2	2	0
41-45	24	8	2	0	1
Total	61	18	6	4	2

Table 9: Analysis of lesions in X-ray according to Age – Left

Age group	Infiltrates	Cavity	Consolidation	Effusion	Hydropneumo thorax
25-30	12	2	3	0	0
31-35	4	0	0	1	0
36-40	9	1	0	0	0
41-45	16	0	0	1	1
Total	41	3	3	2	1

Analysis of lesions according to the age group shows that infiltrates are common in all age groups when compared to other lesions.

Table 10: Analysis of lesions according to blood sugar values – Right

Lesions	ADA Grade			
	N	IFG	IGT	DM
Infiltrates	27 (62%)	2 (50%)	23 (74%)	9 (64%)
Cavity	10 (25%)	1 (25%)	3 (9%)	4 (28%)
Consolidation	4 (9%)	0	1 (3%)	1 (7%)
Effusion	2 (4%)	0	3 (9%)	0
Hydropneumo Thorax	0	1 (25%)	1 (3%)	0
Total	43	4	31	14

Table 11: Analysis of Lesions according to Blood Sugar value – Left

Lesions	ADA Grade			
	N	IFG	IGT	DM
Infiltrates	16 (76.4%)	3 (100%)	14 (82%)	8 (80%)
Cavity	1 (4.7%)	0	1 (5.8%)	1 (10%)
Consolidation	3 (14.2%)	0	0	0
Effusion	1 (4.7%)	0	1 (5.8%)	0
Hydropneumothorax	0	0	1 (5.8%)	1 (10%)
Total	21	3	17	10

Infiltrates dominate as the major lesion in all the ADA grades as shown in the Tables above

Table 12: Statistical analysis of Rural Urban Variation

	Urban	Rural	t value	p value
IGT	0.4516	0.1667	3.5873	0.0005*
DM	0.2419	0.1000	2.1257	0.0356*

The statistical analysis shows that both IGT and DM were common in urban population with the significant p value < 0.05*.

Table 13: Statistical analysis of BMI

	Male	Female	Total
Mean	22.74	22.08	22.76
SD	2.00	1.47	1.83
Range	20-24	20-24	20-24

Mean BMI was slightly above the predicted BMI of South Indian population (18-22). Statistical analysis among ADA grades didn't show any significant difference p value was > 0.05.

Discussion

Present study analyses OGTT results in tuberculous patients. 31.14% had IGT and 17.2% had DM and the total number of patients with abnormal blood sugar values (IFG, + IGT + DM) account for 53.28% of the study group. Recent studies over the past 5 years have shown variable results for IGT in TB.

Bloom (1969)[8] suggested that occult glucose intolerance predisposes to diabetes. Zack et al[9] (1973) suggested that glucose intolerance was not merely a reaction to acute tuberculous infection but rather a prediabetic state. Hadden[10] (1967) suggested malnutrition in tuberculosis as a possible cause. Acute severe stress, fever, inactivity and malnutrition stimulate the stress hormones epinephrine, glucagon and cortisol which raise the blood sugar level (Guptan et al, 2000)[11]. Clinical and sub clinical hypoadrenalism have been described in these patients (Guptan and Shah, 2000)[11]. Plasma level of IL -1 and TNF are also raised in severe illness, which can stimulate anti-insulin responses. Age, co-existing illness and alcoholism also influence the host response (Fernandez et al, 1997)[12].

The increased prevalence of IGT in the present study can be explained by increase in IGT among general population due to reasons like urbanization, sedentary life style, eating habits etc. But the IGT is significantly high in TB population -31% when compared to 14%in normal population and p value is significant <0.05

The present study shows that IGT in tuberculosis patients is two times higher than general population. The prevalence of diabetes mellitus found in this study is 17.21% and is high compared to 13% in the general population of Tamilnadu belonging to the same age group; even through the p value is not significant.

Present study also reveals an important point that IGT was almost equally distributed in the study population regardless of age, whereas DM, was more in >35 age group. It can be derived from these results that prevalence of IGT is increasing among young Indian population, and is also significantly more among the tuberculous patients and they should be followed up as 50% of patients in the IGT group will develop diabetes. IGT is a well-established risk factor for diabetes and coronary artery disease and this fact should be kept in mind.

Of the diabetics detected in this study, 85.7% were above 35 years of age, and the fact that advancing age, favors the coexistence of diabetes and tuberculosis is again proved here.

Male patients were almost twice the number of female patients in this study (81 Vs 41). The gross variation of increased male prevalence for tuberculosis may be related to their increased exposure to tuberculosis and habits like smoking leading to increased susceptibility. Also alcoholism which leads to under nutrition and suppression of immune system may contribute to this malady. But the GTT results didn't show any significant variation according to gender in this study.

Considering the zone of tuberculosis involvement in the study group, a total of 61% of the study group shows upper zone involvement. As far as the lesions are considered, infiltrates were the commonest lesion observed in the study group regardless of blood sugar values.

Older studies have suggested an increased frequency of lower lobe TB as well as greater predisposition to cavitary lesion. This was reported more in the older patients. However studies by Parmer and Beyer have shown that lower lung field involvement is an infrequent location of pulmonary TB, occurring in 7% or less of patients with active pulmonary TB. Infiltrates are reported as predominant lesion in 22.58% by M.K. Jain et al 2003[13].

The average BMI of the patients in the study group was 22.74 in males and 22.08 in females. As BMI >25 was considered as exclusion criteria to eliminate a possible bias due to metabolic syndrome, naturally all the study patients will have BMI < 25, but the average was around 22 and there was no statistical correlation between IGT or DM and increased BMI. This can be explained by the fact that majority of patients attending our hospital belong to low socioeconomic status and the common factor of malnutrition and poor access to medical facilities may account for the above observation and also to the development of hitherto uncommon malnutrition related diabetes in both IGT and normal group. Zack et al[9] (1973) Mugusi et al[14] (1990) also found no significant difference in BMI among the two groups.

50.8% of study population belonged to urban domicile and 49.2% belonged to rural domicile in the present study. IGT and DM was more among urban population. Statistically also the increased prevalence was significant P< 0.05. This process can be explained by overcrowding, life style modification and change in dietary habits promoting the conjoint presence of the brewing double trouble. This again reflects the conclusions of Ramachandran et al[15] regarding prevalence of IGT and DM in urban population[16].

Tuberculosis occurring in the elderly age group has been claimed to be an important indicator of some underlying predisposing cause, the most important of which is diabetes. While diabetes in the elderly tuberculosis patients has received considerable attention in the past, the attention is now being focused more and more towards the younger age groups. It is being realized that perhaps, the important pathogenic factor in the development of tuberculosis, even in the younger age group, could be a pre-diabetic state in some cases at least. These instances, could lead to precipitation of frank diabetes. Such cases might be detected if properly investigated.

A significant group of young tuberculous patients may continue to remain in prediabetic state and some of

these cases even though going into a phase of frank diabetes in the later stage may remain completely undetected. The author tried to analyze the above mentioned fact and it is very well proved by the results of the study.

Limitations of the Study

1. As the inclusion criteria were rigid, the true numbers of cases will be more than the number of cases reported daily during the study period.
2. HbA_1C could not be done due to technical constraints.
3. Follow up of patients in IGT-group was not done because of practical difficulties
4. Target organ damage assessment of those patients detected with diabetes was not done as they were beyond the scope of this study

Conclusions

In view of the increased prevalence of diabetes mellitus in tuberculosis population it is suggested that all tuberculosis patients should be evaluated clinically and biochemically for diabetes mellitus as detection and control of diabetes mellitus will help to achieve better tuberculosis control.

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